



DIMERIC FLUORESCENT POLYPEPTIDES

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BACKGROUND OF THE INVENTION

Fluorescent proteins are widely used in the fields of biochemistry, molecular and cell biology, medical diagnostics and drug screening methodologies (Chalfie et al., 1994, Science 263: 802-805; Tsien, 1998, Ann. Rev. Biochem. 67: 509-544). One property shared by the most useful fluorescent proteins is that they require no host-encoded co-factors or substrates for fluorescence. The proteins therefore retain their fluorescent properties both in isolation from their native organism, and when expressed in the cells of other organisms. This property makes them particularly well suited for a variety of in vivo and in vitro applications. Another major advantage of fluorescent proteins for use in biological systems is that they are indeed proteins, which permits their synthesis, within cells or organisms of interest, avoiding a host of problems relating to the attachment of the label to a protein of interest and/or delivery of labeled proteins into a cell. Not only can the proteins be made within the desired cell or organism, but they also retain their fluorescent properties when expressed as fusions with other proteins of interest, which greatly enhances their utility both in vivo and in vitro.

Fluorescent proteins have been used as reporter molecules to study gene expression in culture as well as in transgenic animals by insertion of fluorescent protein coding sequences downstream of an appropriate promoter. They have also been used to study the subcellular localization of proteins by direct fusion of test proteins to fluorescent proteins, and fluorescent proteins have become the reporter of choice for monitoring the infection efficiency of viral vectors both in cell culture and in animals. Variants of fluorescent proteins exhibiting spectral shifts in response to changes in the cellular environment (e.g., changes in pH, ion flux, or the

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